

In the United States Patent and Trademark Office

Application No.: 10/824,860
Applicants: Modliszewski, et al
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Confirmation No.: 7246
Art Unit: 1615
Docket No.: 60307-USA
Title: HOMOGENEOUS, THERMOREVERSIBLE GEL FILM CONTAINING
KAPPA-2 CARRAGEENAN AND SOFT CAPSULES MADE THEREFROM

Declaration Under 37 C.F.R. § 1.132

I, Kevin Stokes, declare as follows:

I. Background

- A. I am currently a Senior Development Scientist within the FMC Healthcare Ventures unit of FMC BioPolymer and am tasked with the technical development of non-gelatin soft capsule technology. I have been employed with FMC for eleven years in various research and technical support roles. Prior to this I was employed for six years at Vintage Pharmaceuticals, LLC with the final assignment as Supervisor of R&D and Production. My education includes earning a Master's of Science degree in Pharmaceutical Science with a concentration in Pharmaceutics and Bachelor's of Arts degree in Chemistry.
- B. I am familiar with USSN 10/824,860 and the invention claimed and described therein. I am also familiar with the Office Action dated June 16, 2009.
- C. In recent years, I have obtained a significant amount of experience relating to carrageenan films, soft capsule development and manufacture.
- D. The following comparative testing was carried out by me and/or under my direction.

II. Experimental work performed

- A. US 6,949,256 (the "256 Patent") discloses a film forming composition comprising kappa carrageenan in an amount less than 50% of total carrageenan in the composition and further teaches that the amount of kappa carrageenan is desirably less than or equal to 100% of the iota carrageenan (see col. 5, lines 1-6). US 6,375,981 (the "981 Patent") teaches that a combination of kappa carrageenan and iota carrageenan, most preferably in a weight ratio of 1:1, is "especially preferred" (see col. 2, lines 14-16). Example 10 of the '981 Patent tested the flow properties of kappa carrageenan and the 1:1 mixture of kappa carrageenan and iota carrageenan as a measure of the processing advantages thereof, and the '981 Patent teaches in Example 10 that the physical mixture of kappa and iota

carrageenan was found to be preferred. In view of these teachings, the specific purpose of the tests outlined herein was to quantitatively measure the flow properties at various temperatures of the invention as claimed in USSN 10/824,860 (the "present invention") as compared to a physical 1:1 mixture of kappa carrageenan and iota carrageenan. In addition, this work was intended to compare the flow rates of the two tested compositions that differ in carrageenan selection only.

- B. The first composition comprised kappa-2 carrageenan, starch, water, and two plasticizers; glycerin and sorbitol special in accordance with the present invention. The second composition was comprised similarly as the first, except that the kappa-2 carrageenan amount was substituted with a similar amount of a 50:50 physical mixture of kappa carrageenan and iota carrageenan (as described in the '981 Patent to be the preferred composition). Table 1 below is provided to show the materials that were used for each experiment and their composition levels. The formulations were modeled after Examples 8 and 10 of the '981 Patent, except using kappa-2 carrageenan in the sample of the present invention.

- C. Table 1: Sample compositions

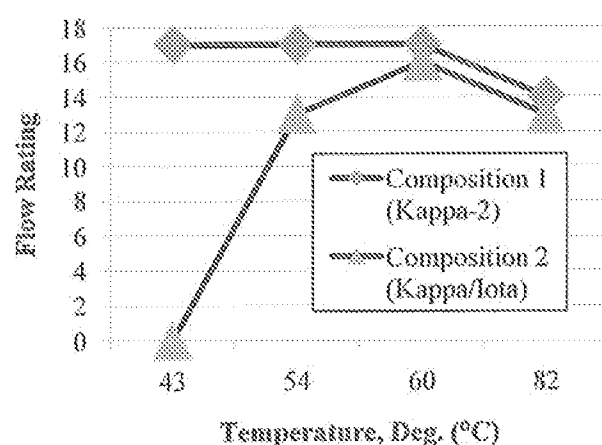
Ingredients	Composition 1 Present Invention	Composition 2 Comparative Sample
Kappa-2 carrageenan	2.3 %	---
Kappa carrageenan	---	1.2%
Iota carrageenan	---	1.2%
Starch	16.0 %	16.0 %
Sorbitol Special	26.0 %	26.0 %
Glycerin	6.7 %	6.7 %
Deionized Water	49.0 %	49.0 %

- D. A laboratory 1.5 Liter double planetary mixer was used to prepare each composition. The processing of these compositions involved mixing the ingredients together while heating the vessel contents under negative pressure. The resulting hot mass that was obtained from each experiment was immediately transferred into four preheated glass sample jars that had been stored for an hour in an oven set to 82°C to condition. A different sample jar from each of these experiments was removed at the desired oven temperature and used to measure the flow rate. Each composition targeted 43% solids with the powder weights adjusted for water content and the remaining composition as deionized water.
- E. The flow of each composition sample conditioned at the desired oven temperature was measured using a Daniel Flow Gauge. This is an apparatus available from Elcometer® that is constructed of a stainless steel plate affixed perpendicular to a concave trough. The plate is scribed with graduated lines that are spaced evenly apart to indicate the distance that a material flows across the plate when the reservoir is lifted to the vertical position. For these two experiments, the flow gauge was used at room temperature.
- F. The flow rating for each of the four samples that were measured from these two experiments were compared graphically in Figure 1. A high value flow rating indicates a

readily flowing material. A zero value flow rating indicates the sample could not be removed from the jar and did not flow.

- G. There was a noticeable difference between the composition's physical structures once they had cooled to ambient temperature. Composition 1, which was made with kappa-2 carrageenan, remained malleable to the touch whereas Composition 2, which was made with physical mix of kappa and iota carrageenan, had formed a rigid structure that was easily lifted off the apparatus once it had cooled. These differences were apparent with the remaining samples that were tested at lower oven temperatures.

- H. Figure 1: Comparison of flow ratings



III. Conclusion

- A. The two compositions behaved significantly differently at similar test conditions. The substitution of kappa-2 carrageenan for an equal amount of a physical mixture of kappa and iota carrageenan in similarly prepared and concentrated compositions did not result in samples with similar flow ratings at lower oven storage temperatures. The kappa-2 carrageenan sample of the present invention throughout the tested temperature range had a high flow rating (indicating a readily flowing material), whereas the sample containing the physical mixture decreased in flow at the lower temperatures to a point of no flow at the lowest tested temperature.
- B. In addition, the sampled material that remained on the flow apparatus after testing and cooling were physically different. The samples that were made with kappa-2 carrageenan remained soft and malleable whereas those made with the physical mixture of kappa and iota carrageenan became rigid enough to be removed from the apparatus in one piece.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were

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made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful and false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: November 5, 2009

Signed: Kevin M. Stokes

Print Name: Kevin Stokes